



DOH 343-071 January 2012

For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

Diagnosis of Latent Tuberculosis Infection

CONTENTS

Forms Used in this Section	6.2
Quick Start Check List	6.3
Introduction.....	6.5
Purpose.....	6.5
High-Risk Groups	6.5
Diagnosis of Latent Tuberculosis Infection.....	6.7
Interferon Gamma Release Assay (IGRA).....	6.7
Mantoux tuberculin skin testing	6.9
Candidates for Mantoux tuberculin skin testing	6.9
Administration of the tuberculin skin test	6.12
Measurement of the tuberculin skin test	6.14
Interpretation of the tuberculin skin test.....	6.15
Human immunodeficiency virus screening	6.17
Follow-up activities.....	6.17
Chest radiography.....	6.17
Resources and References	6.20

Forms Used in this Section

- [Chart Audit Tool](#)
- [Contact Investigation](#)
- [Contact Investigation Instructions](#)
- [Drug-O-Gram](#) (TPCHD)
- [LTBI Testing/Recording](#)
- [Protocol and Standing Orders](#) (SHD)
- [QFT: TB Control Guidelines for Public Health Staff](#) (Thurston County)
- [Symptom Screen](#) (Georgia)
- [Tuberculosis Screening Guidelines](#)

Quick Start Check List: Diagnosis of Latent Tuberculosis Infection

This check list is designed to assist public health nurses in evaluating a patient for latent tuberculosis infection. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:

Washington State TB Services

Mailing address: P.O. Box 47837 Olympia, WA 98504

Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
<p>Determine whom to test</p> <ul style="list-style-type: none"> • Submit the "TB Contact Investigation Form" to WA State TB Services within 2 weeks 	<p>Instructions:</p> <p>For persons who are not part of a contact investigation: Targeted Tuberculin Testing</p> <ul style="list-style-type: none"> • http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf <p>Mantoux Tuberculin Skin Test</p> <ul style="list-style-type: none"> • http://cdc.gov/tb/education/mantoux/default.htm <p>For persons who are contacts: Contact Investigation Guidelines</p> <ul style="list-style-type: none"> • www.cdc.gov/mmwr/pdf/rr/rr5414.pdf • Symptom Screen (Georgia) • Protocol and Standing Orders (SHD) <p>Forms:</p> <ul style="list-style-type: none"> • Contact Investigation <ul style="list-style-type: none"> ○ Instructions
<p>Conduct tuberculin skin testing:</p> <ul style="list-style-type: none"> • Place and measure tuberculin skin tests (TST's) • Interpret TSTs: • 5 mm is positive for persons who are contacts or immunosuppressed • 10 mm is positive for persons with recent infection or clinical conditions of increased risk • 15 mm is positive for persons at low risk • Skin test conversion: For persons previously skin tested, an increase in induration of 10 mm or more within a two-year period is classified as a conversion to positive 	<p>Instructions:</p> <p>Mantoux Tuberculin Skin Test</p> <ul style="list-style-type: none"> • http://www.cdc.gov/tb/education/Mantoux/default.htm • Mantoux Tuberculin Skin Test (manual) (6.9) • Candidates for Mantoux Tuberculin Skin Test (6.10) <p>For diagnosis of latent TB infection (LTBI), improved blood tests called interferon gamma release assays (IGRAs) are available. IGRAs (10.23) are available in Washington State.</p> <ul style="list-style-type: none"> • IGRA (10.23) • QFT: TB Control Guidelines for Public Health Staff (Thurston County) • LTBI Testing/Recording

Tasks for Diagnosis of Latent Tuberculosis Infection	Instructions and Forms
<p>Conduct tuberculin skin testing (cont):</p> <ul style="list-style-type: none"> <input type="checkbox"/> A positive reaction to tuberculin in a bacille Calmette-Guérin-vaccinated person indicates infection with Mycobacterium tuberculosis when the person tested • Is a contact of another person who has infectious tuberculosis (TB) • Resided in a country with high prevalence of TB • Had continuous exposure to populations in which the prevalence of TB is high 	<p>Instructions:</p> <p>The CDC has released “Severe Isoniazid- Associated Liver Injuries Among Persons being Treated for Latent Tuberculosis Infection,” available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5908a3.htm</p> <p>Review the “Tuberculosis Infection Control Program Model Policies for Chemical Dependency Treatment Agencies in Washington State,” available at http://www.dshs.wa.gov/pdf/dbhr/certforms/TBPolicy.pdf</p> <p>Forms:</p> <ul style="list-style-type: none"> • Chart Audit Tool
<p>Screen for human immunodeficiency virus (HIV) in the following persons who test positive with TST or IGRA:</p> <ul style="list-style-type: none"> • Screen all persons in the following groups: • Persons at risk for HIV • Persons younger than 5 years, or • Persons who have a clinical condition such as silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g., leukemia’s and lymphomas), other specific malignancies (e.g., carcinoma of the head or neck and lung), weight loss of greater than 10% body weight, gastrectomy and jejunoileal bypass 	<p>Instructions:</p> <ul style="list-style-type: none"> • Targeted Tuberculin Testing http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf
<p>Exclude active pulmonary disease:</p> <ul style="list-style-type: none"> • Obtain chest radiographs for patients with positive TST results. Chest radiographs are indicated for all persons being considered for treatment of latent TB infection (LTBI) 	
<p>Determine whether to treat the patient for LTBI</p>	<p>Instructions:</p> <ul style="list-style-type: none"> • Targeted Tuberculin Testing http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf
<p>Follow up patients who are contacts in a contact investigation</p>	<p>Instructions:</p> <ul style="list-style-type: none"> • Contact Investigation Guidelines http://www.cdc.gov/mmwr/pdf/rr/rr5414.pdf
<p>Assure that all persons with abnormal chest x-rays and/or symptoms of TB disease are evaluated for TB disease</p> <ul style="list-style-type: none"> <input type="checkbox"/> Submit the “TB Contact Investigation Form” to WA State TB Services within 2 weeks 	<p>Instructions:</p> <p>Targeted Tuberculin Testing</p> <ul style="list-style-type: none"> • http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf <p>Forms:</p> <ul style="list-style-type: none"> • Contact Investigation <ul style="list-style-type: none"> ○ Instructions



To understand the evaluation process in diagnosing TB disease and LTBI, view the “Tuberculosis Screening Guidelines” provided on page [4.6](#).

Introduction

Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Classify patients with latent TB infection (LTBI)
- Diagnose LTBI

In the 2005 guideline “[Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America](#),” one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification of persons with LTBI at risk for progression to TB disease, and treatment of those persons with an effective drug regimen.¹



Contacts are mentioned within this section, but their evaluation and follow-up are covered in more depth in the Contact Investigation section of the manual ([9.1](#)). For information on treatment, refer to the Treatment of Latent Tuberculosis Infection section of the manual ([7.1](#)).

High-Risk Groups

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or for progression to TB disease. Persons in the high-risk groups listed in Table 1: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease are candidates for tuberculin skin testing.

Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country who is also infected with HIV infection is at a much higher risk of having or developing active TB than a US-born individual with HIV infection.

TABLE 1: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE²

For Tuberculosis (TB) Infection	For Progression to TB Disease ³
<ul style="list-style-type: none"> • High-priority contacts such as housemates or coworkers, or contacts of persons who have smear-positive pulmonary or laryngeal tuberculosis (TB) • Infants, children, and adolescents exposed to adults in high-risk categories • Recent immigrants (primarily <5 years) from countries with high incidence of TB (Asian, African, Latin American, and Eastern European countries have TB rates 5–30 times higher than U.S. rates, and an increasing percentage of TB cases in the United States are occurring among immigrants from those countries) • Residents and employees of high-risk congregate settings (e.g., correctional institutions, nursing homes and other long-term care facilities providing care to high-risk residents and clients, and homeless shelters) • Some healthcare workers who serve high-risk clients, especially emergency departments, staff involved in high-risk procedures, and laboratories manipulating TB cultures • Some high-risk racial or ethnic minority populations, defined locally as having an increased prevalence of TB (in Washington State this group includes American Indians and Alaskan Natives) • Some medically underserved, low-income populations as defined locally (e.g., homeless, transient populations) • Persons who inject illicit drugs; any other locally identified high-risk substance abuse users 	<ul style="list-style-type: none"> • Persons with HIV infection • Infants and children aged <5 years • Persons infected with <i>Mycobacterium tuberculosis</i> within the previous 2 years • Persons with a history of untreated or inadequately treated TB disease • Persons with radiographic findings consistent with previous TB disease • Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine) • Persons with any of the following clinical conditions or other immunocompromising conditions: <ul style="list-style-type: none"> • Silicosis • Diabetes mellitus • End-state renal disease (ESRD)/chronic renal failure, hemodialysis • Some hematologic disorders (e.g., leukemia's and lymphomas) • Other malignancies (e.g., carcinoma of head, neck, or lung) • Body weight $\geq 10\%$ below ideal body weight • Prolonged corticosteroid use • Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF-α] antagonists) • Organ transplantation • Gastrectomy • Chronic malabsorption syndromes • Jejunioileal bypass

Source: Adapted from: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9. Also, Tuberculosis Infection Control: A Practical Manual for Preventing TB http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12

Diagnosis of Latent Tuberculosis Infection

The diagnosis of latent tuberculosis infection (LTBI) has traditionally been based upon results of tuberculin skin testing. However, the QuantiFERON[®]-TB Gold (QFT-G) test, QuantiFERON[®]-TB Gold in-tube (QFT[™]) test and the -SPOT[®].TB test, which are whole-blood interferon gamma release assays (IGRAs), are now other options for detecting LTBI.

Use the Mantoux tuberculin skin test (TST) or an IGRA to test for *Mycobacterium tuberculosis* infection. IGRA can be used in all circumstances in which the TST is used, and IGRAs usually can be used in place of (and not in addition to) the TST.⁴



For information on testing methods available in Washington refer to the Laboratory Services Section ([10.1](#))



For a summary of the TB classification numbers, refer to the "[Tuberculosis Classification System](#)" topic in the Surveillance section.

Interferon Gamma Release Assays (IGRA)

Blood assay for *Mycobacterium tuberculosis* (BAMT) is a general term referring to recently developed in vitro diagnostic tests that assess for the presence of infection with *M. tuberculosis*. This term includes, but is not limited to, interferon gamma release assays (IGRAs). The IGRAs currently approved by the Food and Drug Administration (FDA) and available on the market are the QuantiFERON[®]-TB Gold in-tube (QFT[™]) test, which replaces the QuantiFERON[®]-TB Gold (QFT-G) test and the -SPOT[®].TB test. IGRAs can be used in all circumstances in which the TST is used, and the IGRAs usually can be used in place of the TST.⁵ Other cytokine-based immunoassays are under development and may also become useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products, in combination with Centers for Disease Control and Prevention (CDC)-issued recommendations, may provide additional diagnostic alternatives.⁶ The advantages of IGRA, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory, the variability associated with skin test reading can be eliminated.⁷ In addition, IGRA tests appear to be less affected by past bacille of Calmette-Guérin (BCG) vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.⁸ However, the IGTA tests have practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. For the QFT-G test, the blood must arrive at the laboratory less than 12 hours after collection to be incubated with the test antigens, while the lymphocytes are viable.⁹ For a QFT[™] test, the blood specimens are collected directly into the three blood collection tubes, shaken vigorously, and then incubated at the collection site. After incubation, blood collection tubes should be stored no longer than three days prior to centrifugation and laboratory manipulation.



A single IGRA test is used in place of (and not in addition to) the TST in screening of healthcare workers.

Resources for IGRA Testing:

- CDC. “Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC” (*MMWR* 2005;54[No. RR-15]). Available at: <http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf> .
- CDC. “Guidelines for Using the QuantiFERON-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States” (*MMWR* 2005;54[No. RR-15]). Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.htm> .
- CDC. “Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-care Settings, 2005” (*MMWR* 2005;54[No. RR-17]). Available at: <http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf> .
- Curry International Tuberculosis Center. *Tuberculosis Infection Control: A Practical Manual for Preventing TB* (Curry International Tuberculosis Center web site; 2007). Available at: http://www.currytbcenter.ucsf.edu/products/product_details.cfm?productID=WPT-12
- CDC Interferon Gamma Release Assays (IGRA) guidelines, “Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010” (*MMWR* 2010; 59 [No. RR-5];1-25) at <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>.

CDC Interferon-Gamma Release Assays (fact sheet) that will assist you in learning more about IGRAs. <http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm>



For information on available IGRA testing in Washington refer to the Laboratory Services Section ([10.8](#))



For more information regarding QFT healthcare worker guidelines see [QFT: TB Control Guidelines for Public Health Staff](#) (Forms Section)



Find answers to common questions posed by healthcare professionals on the use of QFT at <http://www.cellestis.com/IRM/Company/ShowPage.aspx?CPID=1588&EID=60701344>

Mantoux Tuberculin Skin Testing (TST)

The Mantoux method of tuberculin skin testing is used to detect infection with *Mycobacterium tuberculosis*.

In general, it may take up to 10 weeks after infection for a person to develop a delayed-type immune response to tuberculin which is measurable with the Mantoux tuberculin skin test (TST).¹⁰ During the test, tuberculin is injected intradermally into the skin. The immune system of most persons with tuberculosis (TB) infection will recognize the tuberculin, causing a reaction in the skin. Repeated TSTs do not produce hypersensitivity. Guidelines for interpretation of the TST are found in the CDC Mantoux Tuberculin Skin Test Training Materials Kit at <http://www.cdc.gov/tb/education/mantoux/default.htm>

The size of the measured induration (a hard, dense, raised formation) and the patient's individual risk factors should determine whether TB infection is diagnosed.¹¹ Based upon the sensitivity and specificity of the purified protein derivative (PPD) TST and the prevalence of TB in different groups, three cut-points have been recommended for defining a positive tuberculin reaction:

- Greater than or equal to 5 mm on induration
- Greater than or equal to 10 mm induration
- Greater than or equal to 15 mm of induration¹²



For more information on cut-points for the TST, see the “Interpretation of the Tuberculin Skin Test” topic in this section of the manual (6.16), or Mantoux Tuberculin Skin Test Training Materials Kit at <http://www.cdc.gov/tb/education/mantoux/default.htm>

Candidates for Mantoux Tuberculin Skin Testing

The Mantoux TST can be administered to all persons, including pregnant women,¹³ persons who have previously been vaccinated with bacille Calmette-Guérin (BCG),¹⁴ and human immunodeficiency virus (HIV)-infected persons. However, persons with a documented prior positive TST do not need another TST, and the Mantoux TST should not be administered until four weeks after vaccination with live-virus vaccines.



If the person being tested is a contact, follow the procedures outlined in the Contact Investigation section of the manual (9.1) and Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis at <http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf>

Pregnancy

Tuberculin skin testing is entirely safe and reliable for pregnant women, and pregnant women at high risk for TB infection or disease should be tested. Screen pregnant women for TB infection if they have any of the following conditions:

- Symptoms suggestive of TB disease
- HIV infection
- Behavioral risk factors for HIV
- Medical conditions other than HIV infection that increase the risk for TB disease
- Close contact with a person who has pulmonary or laryngeal TB disease
- Immigration from an area of the world where incidence of TB is high

Bacille Calmette-Guérin Vaccine

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis*. Because their effectiveness in preventing infectious forms of TB has never been demonstrated in the United States, they are not recommended as a TB control strategy in the United States, except under rare circumstances. They are, however, used commonly in other countries. A history of BCG vaccination is not a contraindication for tuberculin skin testing, nor does it influence the indications for a TST. Administer and measure TSTs in BCG-vaccinated persons in the same manner as in those with no previous BCG vaccination.

Bacille Calmette-Guérin Talking Points

1. Tuberculin reactivity caused by BCG vaccination wanes with time but can be boosted with a TST.¹⁵
2. There is no method to distinguish TB tuberculin reactions caused by vaccination with BCG from those caused by mycobacterial infections.¹⁶
3. A diagnosis of *M. tuberculosis* infection should be considered for any BCG-vaccinated person who has TST reaction ≥ 10 mm of induration.¹⁷
4. Treatment for LTBI should be considered for a person who is TST positive and has had previous BCG vaccination if the person is:
 - A contact of a person with infectious TB or
 - Vaccinated and born in or resided in a country of high prevalence of TB or
 - Exposed to persons at risk for TB¹⁸
5. BCG vaccination should be considered for infants and children who reside in high morbidity countries to prevent meningeal TB.¹⁹
6. There is no scientific evidence of protective ability of BCG for preventing pulmonary TB in adolescents or adults.²⁰
7. An IGRA is preferred for testing persons who have received BCG.²¹



The BCG vaccine is not available in the United States. The Vancouver Chest Clinic [655 W. 12th Ave., Vancouver, B.C. phone (604) 660-6108] will provide a BCG vaccine. The client must: a) call for an appt., b) get a baseline TST, c) if TST is negative a medical provider will interview the client and if the client meets their criteria, the medical provider will approve the BCG vaccine.

Anergy Testing

Anergy testing is not routinely recommended in conjunction with TST for HIV-infected persons in the United States.²²

Anergy testing is a diagnostic procedure used to obtain information about the competence of the cellular immune system. Conditions that cause an impaired cellular immune system include HIV infection, severe or febrile illness, measles or other viral infections, Hodgkin's disease, sarcoidosis, live-virus vaccination, and corticosteroid or immunosuppressive therapy. Persons with conditions such as these may have suppressed reactions to a TST even if infected with TB. However, there are no simple skin testing protocols that can reliably identify persons as either anergic or nonanergic and that have been proven to be feasible for application in public health TB screening programs. Factors limiting the usefulness of anergy skin testing include the following:

- Problems with standardization and reproducibility
- Low risk for TB associated with a diagnosis of anergy
- Lack of apparent benefit of treatment for LTBI in groups of anergic HIV-infected persons



For more information on Anergy testing, see http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm?s_cid=rr5417a1_e

Also, see JAMA article "The Case Against Anergy Testing as a Routine Adjunct to Tuberculin Skin Testing", at <http://jama.ama-assn.org/cgi/content/abstract/283/15/2003?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=The+Case+Against+Anergy+Testing+as+a+Routine+Adjunct+to+Tuberculin+Skin+Testing&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>

Documented Prior Positive Tuberculin Skin Test

Persons who have tested positive in the past and can provide documentation of their status should not have another TST. Instead, they should have a TB symptom assessment questionnaire administered to identify any symptoms of TB disease.²³ Persons who are symptomatic should have a chest radiograph performed. See [Tuberculosis Infection Control: A Practical Manual for Preventing TB](#) (appendix E. TB Screening Questionnaire for Healthcare Workers).

Live-Virus Vaccines

The Mantoux TST can be administered in conjunction with all vaccines. However, the measles (MMR) vaccine—and possibly mumps, rubella, varicella, and live attenuated influenza vaccines—may transiently suppress the response to PPD.²⁴ Therefore, if a vaccine containing live virus (e.g., measles, smallpox) has already been given, the TST should be deferred until (or repeated) at least four weeks after the vaccine was administered.

When giving the TST and the MMR, one of the following three sequences should be used:

- Apply the TST at same visit as the MMR
- Delay the TST at least four weeks if the MMR is given first
- Apply the TST first and then give the MMR when the TST is measured²⁵



American Academy of Pediatrics. Pickering LK ed. Red Book: 2003 Report of the Committee on Infectious Diseases. 26th ed. Elk Grove Village, IL; American Academy of Pediatrics 2003:
<http://aapredbook.aappublications.org/content/dtl/2003/1/>

Administration of the Tuberculin Skin Test

The TST should be placed and read by a healthcare worker who has received appropriate training and is following written protocols.

TABLE 2: BEFORE YOU BEGIN TO ADMINISTER A TUBERCULIN SKIN TEST

Before You Begin to Administer a TST	
Review Information	CDC. <i>Mantoux Tuberculin Skin Test Facilitator Guide</i> at http://www.cdc.gov/tb/education/mantoux/default.htm Follow all Infection control procedures (including hand washing before and after the procedure and the use of gloves and a sharps container)

Gather Equipment	<ul style="list-style-type: none"> • Gloves • Alcohol pads or alternative skin cleanser • Safety needle • Tuberculin syringe (Do not pre-draw tuberculin into syringes prior to test.) • Purified protein derivative (PPD) (Tubersol® or Aplisol®: See the warning in the text below in this table.) • Sharps container <p>Note: Date PPD tuberculin vials when opened and discard after 30 days. See the package insert for appropriate storage information.</p>
------------------	---



Read the PPD labels carefully before administering a TST. The packaging of tetanus toxoid-containing vaccines (TTCVs) is similar to Tubersol® and Aplisol®, and all are refrigerated. See the CDC’s “Errors Involving Mix-up of Tuberculin Purified Protein Derivative and Vaccine Products” (*TB Notes Newsletter*. 2005;No. 1).

How to Administer a Tuberculin Skin Test

1. Obtain the patient’s written consent if required by the provider’s agency/institution
2. Inject air into the vial air space (not into the solution). Injection of air into the air space in the vial prevents creation of negative pressure within the vial, allowing the antigen to be withdrawn easily. Injecting air into the solution creates bubbles and may interfere with withdrawing the correct amount of antigen.²⁶The injection should be placed on the palm-side-up surface of the forearm, about two to four inches below the elbow. Your local institutional policy may specify the right or left forearm for the skin test. The area selected should be free of any barriers to placing and reading the skin test, such as muscle margins, heavy hair, veins, sores, tattoos, or scars.
3. After choosing the injection site, clean the area with an alcohol swab by circling from the center of the site outward. Allow the site to dry completely before giving the injection.
4. Using a disposable tuberculin safety needle and syringe, inject 0.1 ml of PPD tuberculin containing 5 tuberculin units (TU) intradermally with the needle bevel facing upward. Because some of the tuberculin solution can adhere to the inside of the plastic syringe, the skin test should be given as soon as possible after the syringe is filled.
5. The injection should produce a discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter. **Note:** If a 6- to 10-mm wheal is not produced, repeat the test on the opposite arm or the same arm, 2 inches from the original site.
6. Record the date and time of TST administration, location of injection site, dose, name of person who administered the test, the name and manufacturer of the tuberculin product used, lot number, expiration date, and reason for testing.²¹

Measurement of the Tuberculin Skin Test

A trained healthcare worker should read the TST 48 to 72 hours after the intradermal injection. Patients should never be allowed to read their own TSTs.²²

- A positive reaction can be measured anytime after 48 hours.
- If the results appear negative and more than 72 hours have passed, the test should be repeated. It can be repeated immediately or one to three weeks later if two-step testing is required for employment.



Refer to the topic entitled “Two-Step Tuberculin Skin Testing” in the Infection Control section of the manual ([11.13](#)) and Guidelines for Preventing Transmission of Mycobacterium Tuberculosis in Health-Care Settings at <http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf>



Before you measure a TST, review information in the CDC’s *Mantoux Tuberculin Skin Test Facilitator Guide* at <http://www.cdc.gov/tb/education/mantoux/default.htm>

How to Measure a Tuberculin Skin Test

1. Measure the TST site crosswise to the axis of the forearm (from the thumb side of the arm to the little finger side of the arm or vice versa).
2. Induration is a hard, dense, raised formation. Measure only induration hardness and not swelling around the site of the injection. Do **not** measure erythema (redness). A TST with erythema, but no induration, is a negative TST (nonreactive.)
3. Record the test result in mm, not as “positive” or “negative.” An exact reading in mm may be necessary to interpret whether conversions occur on a subsequent test. Record a TST with no induration as “0 mm.” Where there is induration, do not round off the reading, but record it exactly as read.
4. Report adverse reactions to a TST (e.g., blistering, ulcerations, necrosis) to the FDA’s MedWatch Program at 1-800-FDA-1088, or via the Internet at <http://www.fda.gov/Safety/MedWatch/default.htm>

Interpretation of the Tuberculin Skin Test

TSTs should be interpreted by a trained healthcare worker. Use Table 3 below to interpret TSTs.



Call the local health jurisdiction regarding TST reactions when interpretation and medical follow-up are unclear.



Before you interpret a TST, review information in the CDC's *Mantoux Tuberculin Skin Test Facilitator Guide* at <http://www.cdc.gov/tb/education/mantoux/default.htm>.

How to Interpret a Tuberculin Skin Test

Use the table below to determine when a reaction is positive.

TABLE 3: POSITIVE TUBERCULIN SKIN TEST REACTIONS

Induration Size	Considered Positive For:
5 mm or more	<ul style="list-style-type: none"> Persons with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) Recent contacts to an infectious case of tuberculosis (TB) disease Persons with fibrotic lesions on chest radiograph consistent with healed TB Persons with organ transplants or other immunosuppressed persons (such as those receiving the equivalent of >15 mg/day of prednisone for >1 month) Persons receiving treatment with tumor necrosis factor-alpha (TNF-α) antagonists
10 mm or more	<ul style="list-style-type: none"> Foreign-born persons recently arrived (within 5 years) from countries with a high TB incidence or prevalence (e.g., most countries in Africa, Asia, Latin America, Eastern Europe, the former USSR, or from refugee camps) Persons who inject drugs or use other high-risk substances, such as crack cocaine Alcoholics Residents and employees in high-risk, congregate settings (e.g., correctional institutions; long-term residential care facilities, such as nursing homes, mental institutions, etc.; hospitals and other healthcare facilities; homeless shelters; and refugee camps) Mycobacteriology laboratory personnel Persons with other medical conditions that increase the risk of TB disease Children younger than 5 years of age, or children and adolescents exposed to adults in high-risk categories
15 mm or more	<ul style="list-style-type: none"> Persons with no known risk factors for TB

When interpreting TST results, be aware of the following:

Skin test conversions: For persons previously skin tested, an increase in induration of 10 mm or more within a two-year period is classified as a conversion to positive.

False-negative reactions may be due to the following:

- Anergy



See “Anergy Testing” (6.11) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual and Guidelines for Preventing Transmission of Mycobacterium Tuberculosis in Health-Care Settings at <http://www.cdc.gov/mmwr/pdf/rr/rr5417.pdf>

- Recent TB infection (within the past 8 weeks) since the TST may not yet show positive
- Very young age (less than 6 months of age, because the immune system is not fully developed)
- Overwhelming TB disease
- Vaccination with live viruses (e.g., measles, mumps, rubella, varicella, oral polio, or yellow fever).



TB skin testing should be done either on the same day as vaccination with live virus or at least four weeks after vaccination.



See “Live-Virus Vaccines” (6.12) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual.

- Some viral infections (measles, mumps, chickenpox, or HIV)
- Corticosteroids or other immunosuppressive agents given for two or more weeks

False-positive reactions may be due to the following:²³

- Nontuberculous mycobacteria (NTM) or mycobacterium other than tuberculosis (MOTT)
- BCG vaccination



See “Bacille Calmette-Guérin Vaccine” (6.10) under “Candidates for Mantoux Tuberculin Skin Testing” in this section of the manual.

Human Immunodeficiency Virus Screening

Voluntary counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. HIV counseling and testing has also been recommended for contacts of persons with TB.²⁷

The Centers for Disease Control and Prevention (CDC) recommends the following:

- HIV screening for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
- Routine HIV testing for persons suspected of having TB disease and contacts to TB patients
- Persons at high risk for HIV infection should be screened for HIV at least annually²⁸

Follow-Up Activities

After testing, complete the following tasks



If the person has signs or symptoms of TB, evaluate for TB disease as described in the “Diagnosis of Tuberculosis Disease” topic in the Diagnosis of Tuberculosis Disease section of the manual ([4.1](#)).



If the person is a contact, follow the procedures for testing and evaluation in the Contact Investigation section of the manual ([9.1](#)).



If the person is a participant in two-step screening, refer to the topic entitled “Two-Step Tuberculin Skin Testing” in the Infection Control section of this manual of the manual ([11.13](#)).



If the TST result is positive, an interview and symptom check and a chest radiograph should be obtained for the patient.

Chest Radiography (X-ray)

All individuals being considered for LTBI treatment should undergo a chest radiograph to rule out pulmonary TB disease. For information on how to classify TB, see the “Tuberculosis Classification System” ([2.7](#)) in the Surveillance section of the manual. Refer to Table 4 which follows to determine when to obtain a chest radiograph and what follow-up is required for chest radiograph results.

A posterior-anterior radiograph of the chest is the standard view used for the detection and description of chest abnormalities in adults. In some instances, other views (e.g., lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.



Children younger than 5 years of age should have posterior-anterior and lateral radiographs performed.²⁵



For more information on chest radiographs, refer to the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (Curry International Tuberculosis Center Web site; 2006) at <http://www.currytbcenter.ucsf.edu/radiographic/>.



For persons recently exposed to TB, follow the procedures for testing and evaluation in the Contact Investigation section of the manual ([9.1](#)).



Pregnant women with a positive TST or IGRA should have a shielded chest radiograph. If the pregnant woman is asymptomatic and in the first trimester of pregnancy, the chest radiograph may be postponed until the second trimester²⁹.

TABLE 4: TARGETED TESTING FOR LATENT TUBERCULOSIS INFECTION: WHEN CHEST RADIOGRAPHS ARE REQUIRED AND HOW TO FOLLOW UP ON RADIOGRAPHY RESULTS

Signs or Symptoms of TB Disease?	TST or IGRA/QFT-G Result?	Recent Exposure to Infectious TB?	Chest Radiograph?	Follow-up Action
Yes	Positive or negative	Yes or no	Normal or abnormal	<ul style="list-style-type: none"> Classify as Class 5. Evaluate for TB disease.
No	Negative	No	CXR not recommended unless the patient has HIV infection or other forms of immunosuppression are present	<ul style="list-style-type: none"> Classify as Class 0. Refer to the Diagnosis of Tuberculosis Disease section (4.1)
No	Positive	No	Normal	<ul style="list-style-type: none"> Classify as Class 2. Consider treatment for LTBI. Refer to the Treatment of Latent Tuberculosis Infection section (7.1)
			Abnormal: Noncalcified fibrotic lesions suggestive of old, healed TB; comparison film available and stable	<ul style="list-style-type: none"> Classify as Class 4 or 5. Consider evaluating for TB disease. Refer to the Diagnosis of Tuberculosis Disease section (4.1)
			Abnormal: Consistent with TB disease; no comparison film	<ul style="list-style-type: none"> Classify as Class 3 or 5. Evaluate for TB disease. Refer to the Diagnosis of Tuberculosis Disease section (4.1)
<p>Definitions of abbreviations: CXR = chest radiograph/x-ray; HIV = human immunodeficiency virus; IGRA = interferon gamma release assay/ QuantiFERON®-TB Gold (QFT-G); LTBI = latent tuberculosis infection; TB = tuberculosis; TST = tuberculin skin test.</p>				

Resources and References

Resources

- ATS, CDC, IDSA. “Diagnostic Standards and Classification of Tuberculosis in Adults and Children” (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: <http://www.cdc.gov/tb/publications/PDF/1376.pdf> .
- CDC. *Core Curriculum on Tuberculosis (2011)* [Division of Tuberculosis Elimination Web site]. November 2011. Available at <http://www.cdc.gov/tb/education/corecurr/index.htm> .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>
- Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection *MMWR* June 9, 2000/vol 49/no RR-6 <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm>

References

- ¹ ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54 (No. RR-12):15.
- ² CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9, 22.
- ³ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8–9.
- ⁴ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54 (No. RR-15):52.
- ⁵ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ⁶ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4.
- ⁷ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ⁸ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):50.
- ⁹ CDC. Guidelines for using the QuantiFERON[®]-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- ¹⁰ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):11; CDC, NTCA. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR* 2005;54(No. RR-15):13; County of Los Angeles Tuberculosis Control Program. *Tuberculosis Control Program Manual: 2003 Edition*:2-1. Available at: <http://www.lapublichealth.org/tb/TBManual/TBmanual.pdf> . Accessed January 10, 2012.
- ¹¹ Curry International Tuberculosis Center. *Diagnosis and treatment* [Curry International Tuberculosis Center Web site].
- ¹² CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):1–2.
- ¹³ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):49.
- ¹⁴ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):50.
- ¹⁵ Sepulveda RL, Ferrer X, Latrach C, Sorensen, RU. The influence of Calmette-Guérin Bacillus immunization on the booster effect of tuberculin testing in healthy young adults. *Am Rev Respir Dis* 1990;142:24–28.
- ¹⁶ McKay, A, Kraut A, Murdzak C, Yassi A. Determinants of tuberculin reactivity among health care workers: interpretation of positivity following BCG vaccination. *Can J Infect Dis* 1999;10:134–139.

-
- ¹⁷ CDC. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm> Accessed January 10, 2012.
- ¹⁸ CDC. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm> . Accessed January 10, 2012.
- ¹⁹ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49[No. RR-6]:11.
- ²⁰ CDC. Core Curriculum on Tuberculosis (2000) [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: http://www.cdc.gov/nchstp/tb/pubs/corecurr/Chapter9/Chapter_9_ Interpretation.htm . Accessed June 25, 2009; Smith PG. Case-control studies of the efficacy of BCG against tuberculosis. In: International Union Against Tuberculosis, ed. Proceedings of the XXVIth IUATLD World Conference on Tuberculosis and Respiratory Diseases. Singapore: Professional Postgraduate Services International 1987:73–9.
- ²¹ CDC. Updated Guidelines for Using Interferon Gamma Release Assays to Detect Mycobacterium tuberculosis infection. *MMWR* 2010; 59 (No. RR-05): 1-25.
- ²² CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed January 10, 2012.
- ²³ CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):53.
- ²⁴ CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 9th ed. Washington, DC: Public Health Foundation; 2006:24–25,143.
- ²⁵ CDC. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 9th ed. Washington DC: Public Health Foundation;2006:24–25,143.
- ²¹ CDC. Part two: reading the Mantoux tuberculin skin test. *Mantoux Tuberculin Skin Test Facilitator Guide* [Division of Tuberculosis Elimination Web site]. Available online at: <http://www.cdc.gov/tb/education/mantoux/guide.htm> . Accessed January 10, 2012.
- ²² CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed January 10, 2012.
- ²³ CDC. Tuberculin skin testing. In: Chapter 4: testing for TB disease and infection. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed January 10, 2012.
- ²⁴ CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(No. RR-14):1–17.
- ²⁵ CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):25.
- ²⁶ CDC National Center for Health Statistics. Skin test preparation steps: filling syringes. In: Skin Test Preparation Steps: Filling Syringes. *National Health and Nutrition Examination Survey (NHANES) Manual*. Hyattsville, MD: National Center for Health Statistics.
- ²⁷ ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):51.
- ²⁸ CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(No. RR-14):1–17.
- ²⁹ CDC. Immigrant and Refugee Health. Guidelines for Screening Tuberculosis Infection and Disease during the Domestic Medical Examination for Newly Arrived Refugees. Available at <http://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/tuberculosis-guidelines.html>